UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,403	06/20/2005	Jose Manuel Francisco Ochoa	2099.0090000	3497

26111 7590 05/22/2012

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
LOVE, TREVOR M	
ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
05/22/2012	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,403	OCHOA, JOSE MANUEL FRANCISCO	
	Examiner	Art Unit	
	TREVOR LOVE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2012*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1,4,6,8 and 11-26* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,4,6,8 and 11-26* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made to Applicant's response filed 03/08/2012.

Claims 1, 4, 6, 8, and 11-26 are pending.

Claims 1, 4, 6, 8, and 11 are currently amended.

Claims 12-26 are newly added.

Claims 1, 4, 6, 8, and 11-26 are currently under consideration.

Rejections Maintained and Made Again – New Grounds in view of Applicant's amendments and newly added claims

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The response filed 03/08/2012 has introduced NEW MATTER into the claims.

As presently amended claims 22-26 recite that the identified excipients are present in amounts which are prefaced by the term "about". Thus, the claim broadly encompasses utilizing amounts which are an unspecified amount above or below said

amounts, which was not previously encompassed by the claims or the specification as originally filed. It is noted that the only support the Examiner could find for any amounts of said excipients was located in examples 1-4 of the instant specification which only identify two (2) amounts for each component.

The response did not point out where support for currently amended claims 22-26 could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore specifically point out the support for any amendments made to the disclosure.").

As presently amended, the claims now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the presently amended claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in the present claims in the specification or claims, as filed, or remove these limitations from the claims in response to this Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 4, 6, 8, and 11-19 are rejected under 103(a) as being unpatentable over Seymour (Managed Care) in view of McCall (Expert Opinion on Pharmacotherapy).

Seymour teaches Glucovance is an oral medication that combines glyburide and metformin hydrochloride, which offer complementary mechanisms for achieving glycemic control in patients with Type 2 diabetes (page 11, first para.). Seymour sets forth clinical study trial results wherein diabetic patients were administered placebo, glyburide 2.5 mg alone, metformin 500 mg alone, glyburide 1.25 mg plus metformin 250 mg, glyburide 2.5 mg plus metformin 500 mg (page 13, col. 1, last full para.). Seymour teaches that combination therapy of glimepiride (Amaryl) tablets and metformin hydrochloride (Glucophage) tablets is known in the art. Specifically, Seymour teaches

conversion guides showing how to switch diabetic patients on a combination of glimepiride (Amaryl) tablets and metformin hydrochloride (Glucophage) tablets to Glucovance (Table 1). In particular, Seymour teaches Glucovance tablets containing a combination of 5 mg glyburide and 500 mg metformin hydrochloride (Glucophage; page 14). Seymour teaches that patients on metformin and glyburide-metformin (5 mg/500 mg) were titrated to up to 4 tablets/day (= 20 mg of glyburide and 2000 mg of metformin hydrochloride, which would be equivalent to 8 mg glimepiride and 2000 mg of metformin hydrochloride based on the conversion factors of Seymour; page 15, last para., Table 2). Seymour teaches that in order to avoid hypolgycemia, the starting dose of Glucovance should not exceed the daily dose of glyburide (or equivalent dose of another sulfonylurea) and metformin already being taken and that the daily dose should be titrated in increments of no more than 5 mg/500 mg up to the minimum effective dose necessary to achieve adequate control of blood glucose (page 14, Table 1, including footnotes; and page 15, Table 2, including footnotes). Seymour teaches that the fixed dose combination of glyburide-metformin hydrochloride offers attendant gains in patient compliance in patients who are switched from polytherapy to fixed dose Glucovance monotherapy (page 16, last para).

Seymour fails to directly teach the instant claimed combinations comprising glimepiride and metformin hydrochloride, or the instant claimed weight ratio.

McCall state that glimepiride is a second generation sulfonylurea for treatment of Type 2 diabetes (abstract). McCall teaches that glimepiride's antihyperglycemic efficacy is equal to other secretagogues such as glyburide (abstract; page 703, col. 1,

introduction section). McCall teach that glimepiride is approved for use as monotherapy and for combination therapy with metformin and with insulin (abstract). McCall teaches that the dose of glimepiride 1-8 mg daily as monotherapy (page 706, col. 2). McCall state that glimepiride has some reasonable comparative data suggesting benefit over glyburide (page 709, col. 2, 3rd para.; page 720, conclusion section). McCall states that choosing a drug such as glimepiride merits serious consideration because it offers convenience, dosing flexibility and relatively low expense while minimizing the common barrier to ideal control and the most common adverse effect of secretagogues, hypoglycemia (page 710, col. 2, last para. to page 711, col. 1, line 20). McCall state that glimepiride appears to have a lower risk of hypoglycemia than glyburide (page 703, col. 2, introduction section).

It would have been obvious to a person of skill in the art at the time the invention was made to substitute the glyburide component in Glucovance as taught by Seymour with glimepiride as taught by McCall for its reduced hypoglycemic adverse effects in treating a patient with type 2 diabetes mellitus (page 709, col. 2, 3rd para.; page 710, col. 2, last para. to page 711, col. 1, line 20; page 720, conclusion section). One would have been motivated to do so because McCall suggest that glimepiride offers certain benefits over other secretagogues such as convenience, dosing flexibility and relatively low expense, while minimizing the common barrier to ideal control and the most common adverse effect of secretagogues, hypoglycemia (page 710, col. 2, last para. to page 711, col. 1, line 20) and glyburide as taught by Seymour et al. is also a secretagogue. Since McCall teach that glimepiride is approved for use as monotherapy

in a dose of 1-8 mg daily, and also for combination therapy with metformin (abstract; page 706, col. 2), and Seymour suggest that patients on glimepiride and metformin hydrochloride wherein both drugs are administered as separate dosage forms may benefit from a fix dose tablet formulation comprising metformin hydrochloride and a secretagogue (i.e. glyburide; page 14), one would reasonably expect to successfully substitute the glyburide component in the fixed dose Glucovance tablet formulation comprising metformin hydrochloride 500 mg with a suitable therapeutic dose of glimepiride, for example, of 1 mg (= relative dose ratio of 1/500 of glimepiride and metformin hydrochloride) to arrive at applicant's claimed fixed weight ratio of glimepiride and metformin hydrochloride of "about 1/500" for use in the treatment of a patient with type 2 diabetes mellitus since Seymour suggest that secretagogue - metformin hydrochloride combinations oral tablets offer complementary mechanisms for achieving glycemic control in patients with Type 2 diabetes (page 11, first para.) and may provide gains in patient compliance (page 16, last para.), particularly patients who a require polytherapy with two separate hypoglycemic agents (page 16, last para) and McCall state that glimepiride appears to have a lower risk of hypoglycemia than glyburide (page 703, col. 2, introduction section). Besides, it is routine in the medical arts to combine drugs that are known to have the same therapeutic utility and both metformin hydrochloride and glimepiride are known hypoglycemic drugs as evidenced by the teaching of Seymour and McCall. The motivation for combining the components flows from their individually known common utility (see In re Kerkhoven, 205 USPQ 1069 (CCPPA 1980).

With respect to claim 1, Seymour teaches tablets comprising metformin hydrochloride in a fixed dose combination with a secretagogue (i.e. glyburide), wherein the weight ratio of the secretagogue (i.e. glyburide) to metformin hydrochloride is 5mg/500mg (page 14) and suggest that patients requiring 2 mg of glimepiride and metformin hydrochloride 1000 mg – 2000 mg per day should receive an equivalent dose of glyburide/metformin hydrochloride of 2.5 mg/500mg (= 1 tablet of Glucovance) twice a day, which should be titrated in increments of 5mg/500mg of glyburide/metformin hydrochloride (= 1 tablet of Glucovance i.e. different strength from the 2.5/500 mg tablet; page 14, Table 1). Hence, one would reasonably expect to successfully modify the weight ratio of the secretagogue (e.g. glimepiride)-metformin hydrochloride components in the tablets of Seymour to arrive at the instant claimed weight ratio amounts depending on the dose amount of each agent required to achieve normoglycemic levels in a patient with type 2 diabetes absent objective evidence to the contrary.

Besides, McCall teaches glimepiride in a dose of 1- 8 mg and Seymour teaches regimens comprising glimepiride 2- 8 mg and metformin hydrochloride 1000-2000 mg per day (page 14, Table 1) and therefore one would expect to select any conventionally known dose amount of each component to formulate a fix dose combination tablet (e.g. 2 mg glimepiride and 1000 mg metformin hydrochloride = 1/500 weight ration; or 4 mg glimepiride and 2000 mg metformin hydrochloride = 1/500 weight ratio). Since the prior art encompasses a fixed dose combination comprising glimepiride to metformin hydrochloride in a weight ratio of 1/500 and the instant claims require a fixed dose

combination of glimepiride to metformin hydrochloride in a weight ratio of about 1/500, one would reasonably expect that the fixed dose combination of the identical instantly claimed components in the same weight ratio would exhibit the same therapeutic properties, including being “a synergistic combination.”

Regarding the preamble of claim 1, Seymour teaches Glucovance tablets and tablets comprising active drugs (e.g. glimepiride and metformin hydrochloride) would reasonably be considered to be solid pharmaceutical compositions.

Regarding claim 4, Seymour teaches tablet formulations comprising metformin hydrochloride 500 mg (Glucophage) and glimepiride (Amaryl; see page 14, Table 1) and McCall teaches glimepiride in doses of 1 mg - 8 mg (page 706, col. 2). Further, tablet formulations are routinely formulated with inert components (e.g. binders) to facilitate the pharmaceutical formulation and therefore one would reasonably expect that the tablets encompassed by the prior art would also contain at least one excipient since excipients (e.g. binders) are routinely added to tablet formulations. Hence, it would have been within the scope of knowledge and skill of an artisan at the time the invention was made to add any suitable excipient to the formulation to render it pharmaceutically desirable absent objective evidence to the contrary.

Regarding claim 6, Seymour teaches metformin hydrochloride 1000 mg and glimepiride 2 mg (page 14, Table 1). The above discussion of the limitation "at least one excipient" in connection with claim 4 is incorporated by reference.

Regarding claim 8, the above discussion of claim 1 is incorporated by reference. Further, it would have been obvious to a person of skill in the art at the time the

invention was made to administer the fixed dose combination of glimepiride and metformin hydrochloride having any suitable weight ratio, including applicant's claimed weight ratio amount to control blood glucose levels. One would have been motivated to do so because Seymour suggest that secretagogue - metformin hydrochloride combinations oral tablets offer complementary mechanisms for achieving glycemic control in patients with Type 2 diabetes (page 11, first para.) and may provide gains in patient compliance (page 16, last para.).

Regarding claim 11, Seymour teaches that the daily dose of a fixed dose combination comprising administering a secretagogue (e.g. glyburide) should be titrated in increments of no more than 5 mg/500 mg up to the minimum effective dose necessary to achieve adequate control of blood glucose (page 14, footnotes) such that one would reasonably expect to manipulate the relative dose amounts of glimepiride and metformin hydrochloride of the tablet composition encompassed by the prior art, including arriving at applicant's claimed dose amounts, and administer said fixed dose amounts (e.g. glimepiride 2 mg and metformin hydrochloride 1000 mg) to a patient with type 2 diabetes to achieve adequate control of blood glucose in a patient in said patient based on the conventionally known doses of each agent as taught by Seymour absent objective evidence to the contrary (pages 14-15, Tables 1-2).

With regard to the newly added limitation that the combination reduced blood glucose levels or glycosylated hemoglobin levels in a patient with type 2 diabetes greater than either component alone, it is noted that said feature is a result of the components of the combination, and as such, is met by the prior art as set forth above.

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

Response to Arguments

Applicant argues in the remarks filed 03/08/2012 that “Seymour and McCall do not teach a composition comprising a synergistic combination of glimepiride and metformin hydrochloride at the specified weight ratios" (see remarks, page 8). Applicant's argument is not found persuasive since McCall teaches that glimepiride can be utilized with metformin hydrochloride, and Seymour teaches that the use of a combination of glimepiride and metformin hydrochloride is known in the art. Applicant asserts that neither Seymour or McCall identify that the composition is synergistic. Applicant’s argument is not found persuasive. First, it is noted that the prior art teaches the combination. Further, Applicant appears to be asserting that the alleged synergistic effect is not found in the prior art. Applicant's argument is not found persuasive. Specifically, it is first noted that the prior art teaches combining the two active components. Further, it is noted that Applicant's specification asserts that two known diabetic drugs (metformin and glimepiride) do not have positive effects for diabetics (see Remarks, table on page 14). Additionally, the evidence supporting non-obviousness is weighed against evidence in favor of obviousness. In view of the amount of evidence in favor of obviousness, Applicant's argument is not found persuasive.

Applicant further argues that one would not have been motivated to substitute glimepiride for glyburide in combination with metformin hydrochloride since as of the

date provided by Applicant's exhibit 1 (Miller et al, Diabetes Care, 23:444-448, 2000), i.e., 2001, sulfonylureas such as glimepiride, were still being tested in combination with metformin hydrochloride for compliance with ADA (American Diabetes Association) guidelines (see remarks, page 11). It is noted that Applicant asserting on the record that as of over a year before the filing date of the PCT application that metformin and sulfonylureas (such as glimepiride) were being combined and tested. Furthermore, Applicant's argument based on said admission is not found persuasive since the prior art which provides motivation for the combination of references has earlier filing dates when compared to the instant Application.

Applicant further argues that "at best [the prior art] provide an extremely large number of potential options upon which one of ordinary skill in the art could combine to arrive at a synergistic combination of glimepiride and metformin having the specified weight ratios" (see remarks, page 11). Applicant's argument is not found persuasive since the art is being relied upon for what it would have reasonable conveyed to one of ordinary skill in the art at the time the invention was made. Further, it is noted that MPEP 2123(I) states: "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). […] A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft*

Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also *Upsher-Smith Labs. v. Pamlab, LLC*, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005)".

Applicant further argues that "[e]ven if *prima facie* obviousness were established, evidence of unexpected results and commercial success exists that would overcome such a rejection" (see Remarks, page 13). Applicant provides evidentiary documents in support of the alleged unexpected results. Applicant's arguments and evidence have been fully considered and are not found persuasive. It is first noted that evidence of unexpected results and commercial success does not necessarily overcome any and all rejections based on *prima facie* obviousness. Unexpected results and commercial success, and evidence in support thereof, is considered in determining the appropriateness of a rejection based on *prima facie* obviousness. In the instant case, though Applicant has provided several references in support thereof, the rejection is still proper. Specifically, Applicant's evidence does not overcome the clear teachings in Seymour that ratios of 1/500 of glimepiride to metformin hydrochloride were present in the art (see Seymour, table 1). The fact that Seymour acknowledges that current daily dosages of glimepiride include 2, 4, and 8 mg and daily dosages of metformin hydrochloride include 1000, 1500, and 2000 mg provides clear evidence that said amounts were known in said ratios, and the combination of glimepiride and metformin hydrochloride is clearly set forth as a viable option in both Seymour and McCall. Therefore, Applicant's arguments and evidentiary references are not found persuasive. It is noted that Seymour directly identifies the use of 2 mg glimepiride in combination

with 1000 mg of metformin hydrochloride (ratio of 1:500). Therefore, Applicant's evidence is not found persuasive.

Claims 20-26 are rejected under 103(a) as being unpatentable over Seymour (Managed Care) in view of McCall (Expert Opinion on Pharmacotherapy) as applied to claims 1, 4, 6, 8, and 11-19 above, and further in view of Gatlin et al (U.S. Patent number 6,559,188).

The teachings of Seymour and McCall are set forth above.

Seymour in view of McCall, while teaching the presence of glimepiride and metformin hydrochloride, fails to directly identify which excipients are present.

Gatlin teaches a composition comprising an active agent. Said active agent can be glimepiride (see column 3, lines 54-67 and column 24, lines 50-67), and can also be metformin hydrochloride (see entire document, for instance, column 24, lines 33-49). The excipients for the composition of Gatlin are exemplified as being a combination of microcrystalline cellulose, povidone, croscarmellose sodium, magnesium stearate, colloidal silicon dioxide, and an opadry (see entire document, for instance, examples, and particularly example 5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the microcrystalline cellulose, povidone, croscarmellose sodium, magnesium stearate, colloidal silicon dioxide, and an opadry as taught by Gatlin as the excipients of Seymour in view of McCall. One would have been motivated to do so since Gatlin is teaching that said excipients are not only well known in the art

as tableting excipients, but further, that said tableting excipients can be utilized in compositions which comprise glimepiride and metformin hydrochloride. There would be a reasonable expectation of success since Gatlin is teaching that the actives can be glimepiride and metformin hydrochloride, wherein the excipients taught by Gatlin are well known in the art.

With regard to the opadry being opadry clear, it is noted that Gatlin teaches several different colors of opadry, wherein the use of opadry white, pink, yellow, or clear would be an aesthetic feature, and is an art recognized variable. Therefore, depending on the preference of the artisan, one would utilize any one of said opadry colors.

With regard to the limitations directed to the amounts of the povidone, magnesium stearate, and colloidal silicon dioxide, it is noted first that said limitations are rejected under 35 U.S.C. 112 1st paragraph above. Second, it is noted that the term "about" is not quantified in the specification. Third, Gatlin teaches amounts of povidone ranging from 12 to 24 mg, wherein said amounts are deemed to be about 18 and about 36mg as instantly claimed. With regard to the about 3 and about 6mg of magnesium stearate Gatlin teaches 5.7 to 15.2mg, said range is deemed to be about 3 and about 6mg. Finally, with regard to the instant about 1.8 and about 3.8mg of colloidal silicon dioxide Gatlin teaches 6.4 to 12.8mg, said range is deemed to be about 1.8 and about 3.8mg.

Conclusion

No claims allowed. All claims rejected. No claims objected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TREVOR LOVE whose telephone number is (571)270-5259. The examiner can normally be reached on Monday-Thursday 7:30-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TL

/CHERIE M WOODWARD/
Primary Examiner, Art Unit 1647